

## **AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions and listings of claims in the application:

1. (Currently amended) A strain of *M. bovis* BCG-~~or *M. microti*~~, wherein said strain has integrated the DNA fragment RD1-2F9, which comprises 31808 ~~[[pb]]~~ bp of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*), and which is designated as SEQ ID ~~[[No ]]~~NO:1, and which is responsible for enhanced immunogenicity and increased persistence of BCG to the tubercle bacilli.

2-3. (Canceled)

4. (Currently amended) A strain according to ~~claim 4~~claim 72, wherein said strain has integrated a portion of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*), wherein the integrated DNA comprises at least ~~seven~~nine or more genes or fragments thereof selected from the group consisting of Rv3861 (SEQ ID ~~[[No ]]~~NO:4), Rv3862 (SEQ ID ~~[[No ]]~~NO:5), Rv3863 (SEQ ID ~~[[No ]]~~NO:6), Rv3864 (SEQ ID ~~[[No ]]~~NO:7), Rv3865 (SEQ ID ~~[[No ]]~~NO:8), Rv3866 (SEQ ID ~~[[No ]]~~NO:9), Rv3867 (SEQ ID ~~[[No ]]~~NO:10), Rv3868 (SEQ ID ~~[[No ]]~~NO:11), Rv3869 (SEQ ID ~~[[No ]]~~NO:12), Rv3870 (SEQ ID ~~[[No ]]~~NO:13), Rv3871 (SEQ ID ~~[[No ]]~~NO:14), Rv3872 (SEQ ID ~~[[No ]]~~NO:15, mycobacterial PE), Rv3873 (SEQ ID ~~[[No ]]~~NO:16, PPE), Rv3874 (SEQ ID ~~[[No ]]~~NO:17, CFP-10), Rv3875 (SEQ ID ~~[[No ]]~~NO:18, ESAT-6), Rv3876 (SEQ ID ~~[[No ]]~~NO:19), Rv3877 (SEQ ID ~~[[No ]]~~NO:20), Rv3878 (SEQ ID ~~[[No ]]~~NO:21), Rv3879 (SEQ ID ~~[[No ]]~~NO:22), Rv3880 (SEQ ID ~~[[No ]]~~NO:23), Rv3881 (SEQ ID ~~[[No ]]~~NO:24),

Rv3882 (SEQ ID [[No ]]NO:25), Rv3883 (SEQ ID [[No ]]NO:26), Rv3884 (SEQ ID [[No ]]NO:27), and Rv3885 (SEQ ID [[No ]]NO:28).

5. (Currently amended) A strain according to ~~claim 1~~claim 72, wherein said strain has integrated a portion of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*), wherein the integrated DNA further comprises at least ~~one gene or fragment thereof selected from the group consisting of:~~ Rv3867 (SEQ ID [[No ]]NO:10), or a fragment thereof ~~Rv3868 (SEQ ID No 11), Rv3869 (SEQ ID No 12), Rv3870 (SEQ ID No 13), combined with at least one gene or fragment thereof selected from the group consisting of: Rv3871 (SEQ ID No 14), Rv3872 (SEQ ID [[No ]]NO:15, mycobacterial PE), and Rv3873 (SEQ ID [[No ]]NO:16, PPE), Rv3874 (SEQ ID No 17, CFP 10), Rv3875 (SEQ ID No 18, ESAT 6), Rv3876 (SEQ ID No 19), and Rv3877 (SEQ ID No 20).~~

6-11. (Canceled)

12. (Currently amended) A strain according to ~~claim 11~~claim 72, wherein said strain has integrated a portion of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*), wherein the integrated DNA further comprises Rv3872 (SEQ ID [[No ]]NO:15, mycobacterial PE).

13. (Currently amended) A strain according to claim 12, wherein said strain has integrated a portion of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M.*

*canettii*), wherein the integrated DNA further comprises Rv3873 (SEQ ID [[No ]]NO:16, PPE).

14. (Currently amended) A strain according to claim 13, wherein said strain has integrated a portion of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*), wherein the integrated DNA further comprises at least one gene or fragment thereof selected from Rv3861 (SEQ ID [[No ]]NO:4), Rv3862 (SEQ ID [[No ]]NO:5), Rv3863 (SEQ ID [[No ]]NO:6), Rv3864 (SEQ ID [[No ]]NO:7), Rv3865 (SEQ ID [[No ]]NO:8), Rv3866 (SEQ ID [[No ]]NO:9), Rv3867 (SEQ ID [[No ]]NO:10), ~~Rv3868 (SEQ ID No 11)~~, ~~Rv3869 (SEQ ID No 12)~~, ~~Rv3870 (SEQ ID No 13)~~, Rv3878 (SEQ ID [[No ]]NO:21), Rv3879 (SEQ ID [[No ]]NO:22), Rv3880 (SEQ ID [[No ]]NO:23), Rv3881 (SEQ ID [[No ]]NO:24), Rv3882 (SEQ ID [[No ]]NO:25), Rv3883 (SEQ ID [[No ]]NO:26), Rv3884 (SEQ ID [[No ]]NO:27), and Rv3885 (SEQ ID [[No ]]NO:28).

15-17. (Canceled)

18. (Currently amended) A strain according to ~~claim 4~~claim 72, wherein the coding sequence of the integrated gene is in frame with its natural promoter or with an exogenous promoter, such as a promoter capable of directing high level of expression of said coding sequence.

19. (Currently amended) A strain according to ~~claim 4~~claim 72, wherein the said integrated gene is mutated so as to maintain the improved immunogenicity while decreasing the virulence of the strain.

20. (Previously presented) A strain according to claim 18 , wherein said strain only carries parts of the genes coding for ESAT-6 or CFP-10 in a mycobacterial expression vector under the control of a promoter, more particularly an hsp60 promoter.

21. (Previously presented) A strain according to claim 18, wherein said strain carries at least one portion of the *esat-6* gene that codes for immunogenic 20-mer peptides of ESAT-6 active as T-cell epitopes.

22. (Previously presented) A strain according to claim 19, wherein the *esat-6* encoding gene is altered by directed mutagenesis in a way that most of the immunogenic peptides of ESAT-6 remain intact, but the biological functionality of ESAT-6 is lost.

23. (Previously presented) A strain according to claim 19, wherein the CFP-10 encoding gene is altered by directed mutagenesis in a way that most of the immunogenic peptides of CFP-10 remain intact, but the biological functionality of CFP-10 is lost.

24. (Currently amended) An *M. bovis* BCG::RD1 strain ~~strains~~, which has ~~have~~ integrated a cosmid herein referred to as ~~either RD1-2F9 or RD1-AP34~~, which is ~~are~~ contained in the *E. coli* ~~strains~~ strain deposited at the CNCM under the accession number I-2831 ~~and I-2832 respectively~~.

25. (Cancelled)

26. (Currently amended) An *M. bovis* BCG::RD1 strain, which has integrated the insert of the cosmid RD1-2F9 (~ 32 kb), said cosmid ~~corresponding to~~ comprising the region of the *M. tuberculosis* genome AL123456 from ca. 4337 kb to ca. 4369 kb, having the sequence as shown in SEQ ID [[No ]]NO:1.

27-28. (Cancelled)

29. (Currently amended) A method for preparing and selecting an improved *M. bovis* BCG or *M. microti* ~~strains~~ strain defined in ~~claim 1~~ claim 72, comprising a step consisting of modifying said ~~strains~~ strain by insertion, deletion, or mutation in the integrated portion of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*), more particularly in the *esat-6* or *CFP-10* gene, said method leading to a ~~strains~~ strain that are is less virulent for immuno-depressed individuals.

30-42. (Cancelled)

43. (Currently amended) A pharmaceutical composition comprising a strain according to ~~claim 1~~ claim 72 and a pharmaceutically acceptable carrier.

44. (Currently amended) A pharmaceutical composition according to ~~claim 40~~ claim 43 containing suitable pharmaceutically-acceptable carriers comprising excipients and auxiliaries which facilitate processing of the living vaccine into preparations which can be used pharmaceutically.

45. (Currently amended) A pharmaceutical composition according to ~~claim 40~~ or ~~41~~ claim 43 which is suitable for intravenous or subcutaneous administration.

46. (Currently amended) A vaccine comprising a strain according to ~~claim 40~~ claim 72 and a suitable carrier.

47. (Currently amended) A product comprising a strain according to ~~claim 40~~ claim 72 and at least one protein selected from *ESAT-6* and *CFP-10*, or epitope derived thereof for a separate, simultaneous, or sequential use for treating tuberculosis.

48. (Currently amended) The use of a strain according to ~~claim 4~~ claim 72 for preparing a medicament or a vaccine for preventing or treating tuberculosis.

49. (Currently amended) The use of a strain according to ~~claim 4~~ claim 72 as an adjuvant/immunomodulator for preparing a medicament for the treatment of superficial bladder cancer.

50-56. (Cancelled)

57. (Currently amended) The use of a strain according to ~~claim 4~~ claim 72 as a carrier for the expression of a ~~molecule or an~~ heterologous antigen, wherein the strain further comprises a nucleic acid encoding the heterologous antigen ~~that are of therapeutic or prophylactic interest.~~

58-61. (Cancelled)

62. (Currently amended) A strain according to ~~claim 4~~ claim 72, which has integrated a portion of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*), wherein the integrated DNA further comprises at least one gene or fragment thereof selected from the group consisting of Rv3877 (SEQ ID No 20), Rv3878 (SEQ ID [[No ]]NO:21), Rv3879 (SEQ ID [[No ]]NO:22), Rv3880 (SEQ ID [[No ]]NO:23), Rv3881 (SEQ ID [[No ]]NO:24), Rv3882 (SEQ ID [[No ]]NO:25), Rv3883 (SEQ ID [[No ]]NO:26), Rv3884 (SEQ ID [[No ]]NO:27), and Rv3885 (SEQ ID [[No ]]NO:28) in combination with at least one gene or fragment thereof selected from the group consisting of Rv3874 (SEQ ID No 14), Rv3872 (SEQ ID [[No ]]NO:15, mycobacterial PE)[[.]] and Rv3873 (SEQ ID [[No ]]NO:16, PPE), Rv3874 (SEQ ID No 17, CFP-10), Rv3875 (SEQ ID No 18, ESAT-6), Rv3876 (SEQ ID No 19).

63. (Cancelled)

64. (Currently amended) A strain according to ~~claim 1~~claim 72, wherein the strain has integrated a portion of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*), wherein the integrated DNA further comprises at least one gene or fragment thereof selected from the group consisting of Rv3861 (SEQ ID ~~[[No ]]~~NO:4), Rv3862 (SEQ ID ~~[[No ]]~~NO:5), Rv3863 (SEQ ID ~~[[No ]]~~NO:6), Rv3864 (SEQ ID ~~[[No ]]~~NO:7), Rv3865 (SEQ ID ~~[[No ]]~~NO:8), Rv3866 (SEQ ID ~~[[No ]]~~NO:9), Rv3867 (SEQ ID ~~[[No ]]~~NO:10), ~~Rv3868 (SEQ ID No 11), Rv3869 (SEQ ID No 12), Rv3870 (SEQ ID [[No ]]~~NO:13), Rv3880 (SEQ ID ~~[[No ]]~~NO:23), Rv3881 (SEQ ID ~~[[No ]]~~NO:24), Rv3882 (SEQ ID ~~[[No ]]~~NO:25), Rv3883 (SEQ ID ~~[[No ]]~~NO:26), Rv3884 (SEQ ID ~~[[No ]]~~NO:27), ~~[[or]]and~~ Rv3885 (SEQ ID ~~[[No ]]~~NO:28) in combination with at least one gene or fragment thereof selected from the group consisting of ~~Rv3871 (SEQ ID No 14), Rv3872 (SEQ ID [[No ]]~~NO:15, mycobacterial PE), Rv3873 (SEQ ID ~~[[No ]]~~NO:16, PPE), ~~Rv3874 (SEQ ID No 17, CFP-10), Rv3875 (SEQ ID No 18, ESAT-6), Rv3876 (SEQ ID No 19), Rv3877 (SEQ ID No 20), Rv3878 (SEQ ID [[No ]]~~NO:21), and Rv3879 (SEQ ID ~~[[No ]]~~NO:22).

65-71. (Cancelled)

72. (New) A transformed *M. bovis* BCG strain, wherein the strain has integrated a portion of DNA originating from *Mycobacterium tuberculosis* or any virulent member of the *Mycobacterium tuberculosis* complex (*M. africanum*, *M. bovis*, *M. canettii*), wherein the integrated DNA comprises the genes Rv3874 (SEQ ID NO:17, CPF-10), Rv3875 (SEQ ID NO:18, ESAT-6), Rv3868 (SEQ ID NO:11), Rv3869 (SEQ ID

NO:12), Rv3870 (SEQ ID NO:13), Rv3871 (SEQ ID NO:14), Rv3876 (SEQ ID NO:19), and Rv3877 (SEQ ID NO:20), or fragments thereof.